

REMARKS

Status

Upon entry of the amendments, Claims 1-23 and 28-31 will be pending in this application. Claims 24-27 have been canceled without prejudice or disclaimer to resubmission in a later application. Support for the amendments and new claim can be found in the original claims and throughout the specification. No new matter will be added upon entry of the amendments.

The indication of allowed subject matter is acknowledged with appreciation.

Response to Claim Objections

Applicants affirm the election of Group II. Claims have been amended as being drawn to the elected subject matter. Accordingly, the objections to claims 1-12 and 19-27 are believed to be overcome.

Response to Rejections under 35 U.S.C. §112, 1st ¶

Claims 21-27 were rejected under the first paragraph of 35 U.S.C. §112 for allegedly “not reasonably provid[ing] enablement for treating every known thromboembolic disorder, factor VIIa-associated disorder or pharmaceutical compositions comprising any other therapeutic agent beside instant compounds of formula (I) directed to the elected group.” (O.A. of 08/29/2005, p. 2). However, the Examiner acknowledged that the specification is enabled for treating thrombosis using instant compounds of formula (I) directed to the elected group. (O.A. of 08/29/2005, p. 2). Applicants respectfully traverse the non-enablement rejection with regard to claims 21-23 on the grounds that the enablement for treating thrombosis using instant compounds supports the scope of claims 21-23 for treating thromboembolic disorders. While not acquiescing to the non-enablement rejection with regard to claims 24-27, Applicants have canceled claims 24-27 in order to expedite prosecution.

It is worth noting that “the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public”. *TRAINING MATERIALS FOR EXAMINING PATENT*

*APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST PARAGRAPH-
ENABLEMENT OF CHEMICAL/BIOTECHNICAL APPLICATIONS* (available at

<http://www.uspto.gov>). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. *ibid.*

Applicants respectfully submit that there are numerous resources available to the skilled artisan in the field of medicine that provide information about direct correlations between thrombosis and thromboembolism, hence thromboembolic disorders. Applicants here respectfully submit excerpts from two commonly used medical dictionaries (*Stedman's and Dorland's*) and three leading medical textbooks to demonstrate such direct correlations. (*Robbins Pathologic Basis of Disease; Hurst's The Heart; Harrison's Principles of Internal Medicine.*)

By definition, thrombosis is formation or presence of a thrombus (pl. thrombi); clotting within a blood vessel which may cause infarction of tissues supplied by the vessel. *Stedman's Medical Dictionary; Dorland's Illustrated Medical Dictionary.* Thrombus formation and dissolution is a dynamic event characterized by thrombus propagation (growth of a thrombus), dissolution, recanalization of the occluded vessel and organization of the thrombus, and thrombus embolization (dislodge and travel to other sites in the vasculature) (*Robbins Pathologic Basis of Disease*, 6th Edition, p. 127). Simply defined by *Stedman's Medical Dictionary*, thromboembolism is embolism from a thrombus. *Robbins Pathologic Basis of Disease* (p. 129) emphasized the origin of "thromboembolism" came from the fact that almost all emboli (virtually 99%) represent some part of a dislodged thrombus. Unless otherwise specified, embolism should be considered to be thrombotic in origin. (*ibid.* p. 130). Hence, thromboembolism is one of the clinical manifestations of thrombosis. The phrase "thromboembolic disorder", as used in the instant application, would be understood by one of ordinary skill in the art to include diseases caused by a primary thrombus formed at a site of vascular injury or impaired flow (including valves, atria, veins and arteries) or an embolus which is derived from a primary thrombus but has traveled downstream in the blood and lodged at a remote site. Therefore, applicants respectfully submit that the basis for the enablement of

treating thrombosis should fully support claims 21-23 for treating thromboembolic disorders.

Applicants have included herein below a summary of the individual thromboembolic disorders listed in claim 23 that are implicated by thrombosis. While this list is not exhaustive, it provides support for the subject matter taught in instant claim 23 and should obviate the non-enablement rejection.

Chapter 5 in *Robbins Pathologic Basis of Disease* discussed direct correlations between the following disorders and thrombosis: myocardial infarction (p. 124, 125, 126, 129), atherosclerosis (p. 124, 127), peripheral occlusive arterial disease (p. 127, 132), venous thrombosis (p. 127, 129), deep vein thrombosis (p. 125, 129), coronary arterial thrombosis (p. 129), cerebral arterial thrombosis (p. 129) arterial embolism (p. 130), cerebral embolism (p. 129, 130), kidney embolism (p. 130), pulmonary embolism (p. 129, 130).

The importance of thrombosis in acute coronary syndromes is discussed in detail in Chapter 44 of *Hurst's The Heart*, 10th Edition, p. 1373-1374. Unstable angina is one of the subtypes of the acute coronary syndromes. *ibid*, p. 1374. Plaque disruption and thrombus formation/remodeling lead to a variable degree of luminal obstruction to blood flow and can present clinically as stable or unstable angina or acute myocardial infarction or lead to sudden death. *Ibid*, p. 1377. Not all patients with an acute myocardial infarction arrive in the hospital alive. This group of patients is collectively known as victims of 'ischemic sudden death'.

The paragraph entitled "clinical manifestations of ischemic stroke" (chapter 366, *Harrison's Principles of Internal Medicine*, 14th Edition, p. 2327) defines transient ischemic attack (TIA) as a neurological deficit lasting less than 24 hours. The paragraph entitled "a complete stroke" (*Ibid*) states that ischemic strokes are produced by the same pathophysiologic mechanism responsible for TIA. Ischemic stroke, which accounts for about 85% of all strokes, is generally caused by atherothrombosis or embolism of a major cerebral artery. *Stedman's Medical Dictionary*, p 1711.

Thrombophlebitis is defined as venous inflammation with thrombus formation. *Stedman's Medical Dictionary; Dorland's Illustrated Medical Dictionary*.

In summary, given the disclosure in the application and the state of the art of medicine, Applicants assert that the claims to treating thromboembolic disorders are fully enabled. It is requested that the Examiner withdraw these rejections under 35 U.S.C. § 112, first paragraph with regard to claims 21-23.

Response to Rejections under 35 U.S.C. §112, 2nd ¶

Claims 6-10, 21 and 24-26 were rejected under the second paragraph of 35 U.S.C. §112 as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-10 were alleged to have insufficient antecedent basis for the limitation “prodrug” in claim 1. In response, applicants have deleted the limitation “prodrug” in claims 6-10. Hence, it is respectfully requested that this rejection be withdrawn.

Claim 10 was alleged to have insufficient antecedent basis for the limitation “SO₂alkyl or SO₂(phenyl)” for variable X in claim 1. In response, applicants have deleted the limitation “SO₂alkyl or SO₂(phenyl)” in claim 10. Hence, it is respectfully requested that this rejection be withdrawn.

Claim 21 was rejected for the term “thromboembolic disorder” being indefinite since specific disorders are not defined. Definiteness of claim language is analyzed, not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). See also MPEP 2173.02. A claim term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004).

As shown above, applicants respectfully submit that the meaning of the term “thromboembolic disorder” is discernible to one of ordinary skill in the art. Therefore, claim 21 is not indefinite. Hence, it is respectfully requested that this rejection be withdrawn.

Claims 24-26 were rejected as being indefinite. To further prosecution, claims 24-26 have been canceled without prejudice or disclaimer. Accordingly, the rejections are believed to be rendered moot.

The objections and rejections of the claims are believed to be overcome by the amendments and the reasons discussed above. Accordingly, Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited.

Respectfully submitted,

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